REMARKS

Claims 32-36, 39-54 and 78 are in this application. Applicants hereby cancel withdrawn claims 55-77. Applicants herein cancel claim 36, amend claims 32-35 and 54, and add new claim 79.

Claims 32-36, 39-54 and 78 stand rejected under 35 U.S.C. §112, first paragraph as not enabled. The Examiner asserts that the specification does not reasonably provide enablement for "mutants thereof", stating that "the specification provides no correlation between the 'mutant structure' and a specific measurable relationship to the original structure . . . [b]ecause of the unlimited number of mutation [sic.] that are encompassed by the claims". Applicants have amended independent claim 32 and relevant dependent claims to 1) remove the "mutant thereof" language pertaining to the Nef protein component of the fusion protein, and 2) provide additional structural limitations on mutants of the Tat protein component. Support for these structural limitations may be found in the instant specification at page 18, lines 4-13. In particular, Claim 32 now requires that the Tat mutants maintain immunogenic epitopes present on the wild type Tat protein (i.e., unmutated) but be otherwise biologically inactive, and that the mutations occur within specific, well characterized regions of the Tat protein. Accordingly, the claim now provides additional measurable (by well know methods), functional characteristics, as well as significant structural limitations. Applicants respectfully assert that the instant specification enables the full scope of the pending claims.

Claims 32-36, 39-54 and 78 stand rejected as obvious under 35 U.S.C. §103(a) over Schluesener et al. and Hinkula et al., further in view of Gaynor et al., further in view of Berman et al., or further in view of Forsgren. The Examiner states that close inspection of Table IA of Schluessener et al. demonstrates that not all of the Tat-peptides result in tolerance, and since the claims as pending at the time of the earlier Office Action claimed fusion proteins comprising Nef and mutants thereof and the Nef protein could have been so mutated as to now be the EAU peptide, the disclosure of Schluessener et al. anticipates the instant invention. Applicants state that in view of the amendments to the instant claims, the Nef portion of the claimed fusion protein could not possibly represent the EAU peptide disclosed in Schluessener et al.

Moreover, with regard to the data in Table IA, one skilled in the art would be unable to ascertain any role for the Tat peptide in the context of the EAU peptide: the response elicited with toolbox 101 peptide (containing the Tat peptide) is the same as the response

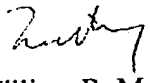
elicited with toolbox 102 peptide (lacking the Tat peptide). Accordingly, it would be clear to one skilled in this art that the Tat peptide, in the context of certain immune epitopes (e.g., EAE and EAN) can induce immune tolerance, but that in the context of certain other epitopes (e.g., EAU), it has no effect on immunogenicity. But there is no evidence in Schluessener et al. that would suggest to one skilled in this art to use the Tat peptide to enhance immunogenecity. Finally, the lack of induction of tolerance to the EAU peptide was unexpected and unexplained (see Schluessener et al., page 262, column 1, first full paragraph). Applicants respectfully maintain that Schluessener et al. teach away from using any portion of Tat as an immunogen and in fact suggest that administration of Tat is an effective means for inducing immune tolerance.

With regard to the Examiner's comments about the Hinkula et al. reference, Applicants' reference in the prior amendment to lack of secretion of the proteins encoded by the Hinkula et al. plasmids was simply to point out, as made clear by Hinkula et al., that Hinkula's peptides do not exist extracellularly and therefore would not be considered by one skilled in this art to exist as a pharmaceutical composition. More importantly, and as pointed out in the prior amendment, Hinkula et al. do not suggest fusing any HIV proteins for any purpose. Accordingly, there is no motivation in either Schluessener et al. or Hinkula et al. to create a fusion protein between Tat and Nef for any purpose. Hinkula et al. success with co-administration of multiple immunogens provides no motivation to combine those immunogens into a single polypeptide molecule (in fact, as pointed out in the previous amendment, Hinkula et al. is concerned solely with DNA immunization and therefore provides no motivation to make any polypeptides at all). Moreover, as stated above, if Schluessener et al. were to provide any motivation to make a fusion protein between Tat and another polypeptide, it would be solely for the purpose of inducing immunological tolerance. This is the only reasonable conclusion one skilled in this art could take away from Schluessener et al. Only in hindsight, and with the benefit of the instant disclosure, does the instant invention become apparent in view of the cited prior art.

In contrast to the Examiner's statement, Applicants respectfully assert that the references do not each teach compositions used to the purpose of immunization to elicit an immune response in a subject. Hence, the combination of Schluessener et al. and Hinkula et al. do not teach or suggest the instant invention. The additional reference cited by the

Examiner are of no consequence in view of the unobviousness of the instant invention in view of the primary references. Accordingly, Applicants respectfully request withdrawal of the 35 U.S.C. § 103(a) rejection and allowance of the instant claims.

Respectfully submitted,



William R. Majarian
Attorney for Applicants
Registration No. 41,173

GLAXOSMITHKLINE
Corporate Intellectual Property - UW2220
P.O. Box 1539
King of Prussia, PA 19406-0939
Phone (610) 270-5968
Facsimile (610) 270-5090

N:\Will\APPS\B-cases\B45110\AF Amendment.doc